Brief Report

Transcritome for Identification of Biomarkers for Diagnosis and Targeted Therapy of Type 1 Diabetes

Felipe Leal Valentim *

Posted Date: 3 November 2025

doi: 10.20944/preprints202510.2463.v1

Keywords: transcriptome; type 1 diabetes; biomarkers; target genes

Brief Report

Transcritome for Identification of Biomarkers for Diagnosis and Targeted Therapy of Type 1 Diabetes

Felipe Leal Valentim

Department of Mechatronics and Mechanical Systems Engineering of the Polytechnic School of the University of São Paulo; felipelealvalentim@usp.br

Abstract

A Transcritptome dataset of whole blood RNA-seq data from type 1 diabetic (T1D) patients and healthy volunteers was deposited on GEO dataset in 2020 (GSE123658). Because of recurrent citations to the transimmunom dataset, read counts at gene level are revised and putative up-regulated biomarkers for T1D diganosis and targeted therapy are presented. We presente TRHDE, GOLGA8I, HBZ, BOLA2B, SPATA22, SEMA6B and FOXQ1 genes as putative biomakers for diagnosis (log2FC ≥1.5 and a padj ≤ 0.05). All together, our result points to GSE123658 dataset as source of biomarkers and therapy target genes.

Keywords: transcriptome; type 1 diabetes; biomarkers; target genes

Introduction

A Transcritptome dataset of whole blood RNA-seq data from type 1 diabetic (T1D) patients and healthy volunteers was deposited on GEO dataset in 2020 (GSE123658). Starting with a protocol for recruitment of participants followed by sample acquisition [1], whole blood RNA from 43 healthy donors and 39 T1D patients were sequenced and the corresponding gene expressions were estimated. Since the upload of the database, GSE123658 was used for in computational experiments in the identification of hub genes related to type 1 diabetes progression [2], and the discovery of gene signatures associated with T Cells and Natural Killer Cells [3]. Moreover, TSPO was identified as the only gene differentially expressed in both conditions T1D (log2FC = 0.504, p = 0.0319) and epilepsy (log2FC = 0.562, p < 0.001) [4]. Finally. three independent diabetes-related GEO datasets - including transimmunom - and found 117 commom T1D genes [5]. Because of recurrent citations to the transimmunom dataset, read counts at gene level are revised and putative up-regulated biomarkers for T1D diganosis and targeted therapy are presented.

Type 1 diabetes (T1D) is an autoimmune disease resultant from β-cell destruction in the pancreascell destruction in the pancreas [6–8]. The molecular mechanisms underlying T1D are known to be related to antigen presentation [9,10], beta cell autoimmunity [11,12] immune tolerance [13,14], T cell response [15–17], chemokine production [18], among other [19–21]. Candidate genes for diagnostic biomarkers can be identified when their expression is high in patients compared to healthy controls. Meanwhile, treatment targets will be found among genes with high interactivity rather than high expression.

Methods

The reads of each sample were then aligned against the Human genome using default parameters of hisat2 for paired reads of forward-cell destruction in the pancreasstranded library. The genome index database was built over the Ensembl Human genome [22] version GRCh37. Next, featureCounts [23] parameters was also adjusted for analysis of paired reads of forward-cell destruction in the pancreasstranded library at gene level. The gene annotation used here was also obtained from Ensembl version GRCh37. The read counts for each sample was merged in a final table

 doi:10.20944/preprints202510.2463.v1

and analyzed with R [25] scripts developed specifically for this dataset. Only protein coding genes located on autosomal chromosomes were further considered.

Results

Only seven up-regulated genes are found to be differently expressed (DE) between T1D and healthy samlples when log2FC ≥ 1.5 and padj ≤ 0.05.

Table 1. Up-regulated biomarkers whose fold change (log2FC) are ≥1.5 and a padj ≤ 0.05 between T1D and healthy samlples.

				healthy		T1D	
Gene name	**log2FC**	**pvalue**	**padj**	**mean**	**sd**	**mean**	**sd**
TRHDE	1.66	1.29E-03	1.35E-02	0.96	1.38	2.97	7.19
GOLGA8I	1.77	8.25E-06	4.95E-04	1.20	1.15	4.26	9.54
HBZ	1.54	1.09E-03	1.21E-02	2.23	3.21	6.64	11.97
BOLA2B	1.95	8.05E-05	2.06E-03	4.67	9.35	17.43	39.83
SPATA22	1.89	3.56E-04	5.58E-03	1.35	2.12	4.60	9.90
SEMA6B	1.65	3.74E-08	1.52E-05	9.73	6.02	29.94	45.24
FOXQ1	2.53	1.97E-05	8.29E-04	1.01	1.89	5.88	17.54

Conclusions

Up-regulated genes whose fold change (log2FC) are ≥1.5 and a padj ≤ 0.05 between T1D and healthy samlples are good candidate for diagnosis biomarkers. Additional molecules can also be found among the down-regulated genes. Furthermore, genes for therapy can be mined by applying criteris to filter out biomarkers with high interactome conectivity.

Declarations: Felipe Leal Valentim FLV submitted the dataset to the GEO database in 2020 (GSE2020123658). FLV was with Unité Immunologie-Immunopathologie-Immunothérapie, INSERM/UPMC for the submission of the dataset. FLV is currently with the Department of Mechatronics and Mechanical Systems Engineering of the Polytechnic School of the University of São Paulo. Scripts to analyse the read counts are found in the github depository : https://github.com/datasciencebioinformatics/TranscriptomeFingerprintAnalysis.

Acknowledgment: I thanks to Adrien SIX and David KLATZMANN for the post-doc oportunity with the data in the Laboratory of Excellence (LabEx) Transimmunom.

References

1. Roberta Lorenzon, Encarnita Mariotti-Ferrandiz, Caroline Aheng, Claire Ribet, Ferial Toumi, Fabien Pitoiset, Wahiba Chaara, Nicolas Derian, Catherine Johanet, Iannis Drakos, Sophie Harris, Serge Amselem, Francis Berenbaum, Olivier Benveniste, Bahram Bodaghi, Patrice Cacoub, Gilles Grateau, Chloe Amouyal, Agnes Hartemann, David Saadoun, Jeremie Sellam, Philippe Seksik, Harry Sokol, Joe-Elie Salem, Eric Vicaut, Adrien Six, Michelle Rosenzwajg, Claude Bernard, David Klatzmann. Clinical and multi-omics cross-phenotyping of patients with autoimmune and autoinflammatory diseases: the observational TRANSIMMUNOM protocol. BMJ Open. 2018 Aug 30;8(8):e021037. doi: 10.1136/bmjopen-2017-021037.
2. G Prashanth, Basavaraj Vastrad, Anandkumar Tengli, Chanabasayya Vastrad, Iranna Kottursheti. Identification of hub genes related to the progression of type 1 diabetes by computational analysis. BMC Endocr Disord. 2021 Apr 7;21:61. doi: 10.1186/s12902-021-00709-6.
3. Na Wang, Guofeng Wang 2, Xiuli Feng, Teng Yang. Identification of Immune Gene Signature Associated with T Cells and Natural Killer Cells in Type 1 Diabetes. Diabetes Metab Syndr Obes. 2024 Aug 9;17:2983–2996. doi: 10.2147/DMSO.S470738.
4. Ruirui Zhang, Shenglin Wang, Sirui Chen, Junqiang Li, Dadong Luo, Kaiyun Jia, Yihe Lian, Tiancheng Wang, Xin Tian. Advancing Understanding of Epilepsy and Type 1 Diabetes Mellitus: A Global Perspective

 doi:10.20944/preprints202510.2463.v1

on Research Trends and Future Directions. J Diabetes Res. 2025 Oct 7:2025:8836992. doi: 10.1155/jdr/8836992. ECollection 2025.

5. Rita T Sousa, Heiko Paulheim. Gene expression knowledge graph for patient representation and diabetes prediction. J Biomed Semantics. 2025 Mar 8;16(1):2. doi: 10.1186/s13326-025-00325-6.
6. Yaíma L Lightfoot, Jing Chen, Clayton E Mathews. Immune-mediated β-cell death in type 1 diabetes: lessons from human β-cell lines. Eur J Clin Invest. Author manuscript; available in PMC: 2013 Jul 8.
7. F Reynier, A Pachot, M Paye, Q Xu, F Turrel-Davin, F Petit, A Hot, C Auffray, N Bendelac, M Nicolino, B Mougin, C Thivolet. Specific gene expression signature associated with development of autoimmune type-I diabetes using whole-blood microarray analysis. Genes Immun. 2010 Apr;11(3):269-78. doi: 10.1038/gene.2009.112. Epub 2010 Jan 21.
8. Tatsuo Tomita. Apoptosis of pancreatic β-cells in Type 1 diabetes. Bosn J Basic Med Sci. 2017 Aug 20;17(3):183-193. doi: 10.17305/bjbms.2017.1961.
9. Jamie L Felton, Damian Maseda, Rachel H Bonami, Chrys Hulbert, James W Thomas. Anti-Insulin B Cells Are Poised for Antigen Presentation in Type 1 Diabetes. J Immunol. 2018 Aug 1;201(3):861-873. doi: 10.4049/jimmunol.1701717. Epub 2018 Jun 2
10. François-Xavier Mauvais, Julien Diana, Peter van Endert. Beta cell antigens in type 1 diabetes: triggers in pathogenesis and therapeutic targets. F1000Res. 2016 Apr 22:5:F1000 Faculty Rev-728. doi: 10.12688/f1000research.7411.1.
11. Mikael Knip, Heli Siljander, Jorma Ilonen, Olli Simell, Riitta Veijola. Role of humoral beta-cell autoimmunity in type 1 diabetes. Pediatr Diabetes. 2016 Jul:17 Suppl 22:17-24. doi: 10.1111/pedi.12386.
12. Astrid Petersmann, Matthias Nauck, Dirk Müller-Wieland, Wolfgang Kerner, Ulrich A Müller, Rüdiger Landgraf, Guido Freckmann, Lutz Heinemann. Definition, Classification and Diagnosis of Diabetes Mellitus. Exp Clin Endocrinol Diabetes. 2018 Jul;126(7):406-410.
13. Chantal Kuhn, Alix Besançon, Sébastien Lemoine, Sylvaine You, Cindy Marquet, Sophie Candon, Lucienne Chatenoud. Regulatory mechanisms of immune tolerance in type 1 diabetes and their failures. J Autoimmun. 2016 Jul:71:69-77. doi: 10.1016/j.jaut.2016.05.002. Epub 2016 May 21.
14. Dan Xu, Suchitra Prasad, Stephen D Miller. Inducing immune tolerance: a focus on Type 1 diabetes mellitus. Diabetes Manag (Lond). 2013 Sep 1;3(5):415-426. doi: 10.2217/dmt.13.36.
15. Adam L Burrack, Tijana Martinov, Brian T Fife. T Cell-Mediated Beta Cell Destruction: Autoimmunity and Alloimmunity in the Context of Type 1 Diabetes. Front Endocrinol (Lausanne). 2017 Dec 5:8:343. doi: 10.3389/fendo.2017.00343. eCollection 2017.
16. Vedran Brezar, Jean-Claude Carel, Christian Boitard, Roberto Mallone. Beyond the hormone: insulin as an autoimmune target in type 1 diabetes. Endocr Rev. 2011 Oct;32(5):623-69. doi: 10.1210/er.2011-0010. Epub 2011 Jun 23.
17. Bart O Roep. The role of T-cells in the pathogenesis of Type 1 diabetes: from cause to cure. Diabetologia. 2003 Mar;46(3):305-21. doi: 10.1007/s00125-003-1089-5. Epub 2003 Mar 22.
18. Adam L Burrack, Tijana Martinov, Brian T Fife. T Cell-Mediated Beta Cell Destruction: Autoimmunity and Alloimmunity in the Context of Type 1 Diabetes. Front Endocrinol (Lausanne). 2017 Dec 5:8:343. doi: 10.3389/fendo.2017.00343. eCollection 2017.
19. Vedran Brezar, Jean-Claude Carel, Christian Boitard, Roberto Mallone. Beyond the hormone: insulin as an autoimmune target in type 1 diabetes. Endocr Rev. 2011 Oct;32(5):623-69. doi: 10.1210/er.2011-0010. Epub 2011 Jun 23.
20. Bart O Roep. The role of T-cells in the pathogenesis of Type 1 diabetes: from cause to cure. Diabetologia. 2003 Mar;46(3):305-21. doi: 10.1007/s00125-003-1089-5. Epub 2003 Mar 22.
21. J Jason Collier, Tim E Sparer, Michael D Karlstad, Susan J Burke. Pancreatic islet inflammation: an emerging role for chemokines. J Mol Endocrinol. 2017 Jul;59(1):R33-R46. doi: 10.1530/JME-17-0042. Epub 2017 Apr 18.
22. Jamie L Felton, Maria J Redondo, Richard A Oram, Cate Speake, S Alice Long, Suna Onengut-Gumuscu, Stephen S Rich, Gabriela S F Monaco, Arianna Harris-Kawano 1, Dianna Perez, Zeb Saeed, Benjamin Hoag, Rashmi Jain, Carmella Evans-Molina, Linda A DiMeglio, Heba M Ismail, Dana Dabelea, Randi K Johnson, Marzhan Urazbayeva, John M Wentworth, Kurt J Griffin, Emily K Sims. Islet autoantibodies as precision

 doi:10.20944/preprints202510.2463.v1

diagnostic tools to characterize heterogeneity in type 1 diabetes: a systematic review. Commun Med (Lond). 2024 Apr 6;4(1):66. doi: 10.1038/s43856-024-00478-y.

23. Adam L Burrack, Tijana Martinov, Brian T Fife. T Cell-Mediated Beta Cell Destruction: Autoimmunity and Alloimmunity in the Context of Type 1 Diabetes. Front Endocrinol (Lausanne). 2017 Dec 5:8:343. doi: 10.3389/fendo.2017.00343. eCollection 2017.
24. Vedran Brezar, Jean-Claude Carel, Christian Boitard, Roberto Mallone. Beyond the hormone: insulin as an autoimmune target in type 1 diabetes. Endocr Rev. 2011 Oct;32(5):623-69. doi: 10.1210/er.2011-0010. Epub 2011 Jun 23.
25. Bart O Roep. The role of T-cells in the pathogenesis of Type 1 diabetes: from cause to cure. Diabetologia. 2003 Mar;46(3):305-21. doi: 10.1007/s00125-003-1089-5. Epub 2003 Mar 22.
26. J Jason Collier, Tim E Sparer, Michael D Karlstad, Susan J Burke. Pancreatic islet inflammation: an emerging role for chemokines. J Mol Endocrinol. 2017 Jul;59(1):R33-R46. doi: 10.1530/JME-17-0042. Epub 2017 Apr 18.
27. Jamie L Felton, Maria J Redondo, Richard A Oram, Cate Speake, S Alice Long, Suna Onengut-Gumuscu, Stephen S Rich, Gabriela S F Monaco, Arianna Harris-Kawano 1, Dianna Perez, Zeb Saeed, Benjamin Hoag, Rashmi Jain, Carmella Evans-Molina, Linda A DiMeglio, Heba M Ismail, Dana Dabelea, Randi K Johnson, Marzhan Urazbayeva, John M Wentworth, Kurt J Griffin, Emily K Sims. Islet autoantibodies as precision diagnostic tools to characterize heterogeneity in type 1 diabetes: a systematic review. Commun Med (Lond). 2024 Apr 6;4(1):66. doi: 10.1038/s43856-024-00478-y.
28. Bart O Roep, Mark Peakman. Antigen targets of type 1 diabetes autoimmunity. Cold Spring Harb Perspect Med . 2012 Apr;2(4):a007781. doi: 10.1101/cshperspect.a007781.
29. Maja Wållberg, Anne Cooke. Immune mechanisms in type 1 diabetes. Trends Immunol . 2013 Dec;34(12):583-91. doi: 10.1016/j.it.2013.08.005. Epub 2013 Sep 18.